

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application.

## **LISTING OF CLAIMS:**

Claims 1-32 (Canceled).

33. (Currently Amended) A method of inducing cellular expansion, comprising the steps of:

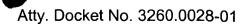
isolating a population of cells to be expanded; and

exposing said cells to a <u>soluble</u> mutant flt3-L polypeptide[[,]] to produce an expanded cell population, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

- 34. (Original) The method of claim 33, wherein the expanded cell population is introduced into a patient.
- 35. (Original) The method of claim 33, wherein the population of cells to be expanded comprises hematopoietic cells.
- 36. (Original) The method of claim 33, wherein the population of cells is also exposed to a growth factor in addition to said flt3-L mutant polypeptide.
- 37. (Original) The method of claim 33, wherein said growth factor is selected from the group consisting of interleukins, colony stimulating factors, and protein kinases.

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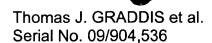
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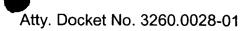


- 38. (Currently amended) A method of expanding a population of cells *in vivo*, comprising the step of administering to a subject a pharmaceutical composition of <u>a soluble</u> mutant flt3-L polypeptide or nucleic acid encoding such polypeptide sufficient to induce the expansion of a target cell population, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 39. (Original) The method of claim 38, wherein the target cell population is isolated from the group consisting of hematopoietic cells, NK cells or dendritic cells.
- 40. (Original) The method of claim 38, wherein the pharmaceutical composition further comprises a growth factor in addition to said flt3-L mutant polypeptides.
- 41. (Original) The method of claim 40, wherein said growth factor is selected from the group consisting of interleukins, colony stimulating factors and protein kinases.
- 42. (Currently amended) A method of modulating an immune response in a subject, said method comprising administering to said subject a therapeutically effective amount of a pharmaceutical composition comprising a soluble flt3-L mutant polypeptide, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) or nucleic acid encoding such polypeptide.
- 43. (Currently amended) A method of treating an immune disorder in a subject, said method comprising administering to said subject a therapeutically effective



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amount of a pharmaceutical composition comprising a <u>soluble</u> flt3-L mutant polypeptide, <u>wherein said polypeptide comprises a substitution at one or more residues</u>

<u>corresponding to amino acid position 24 of the full length human wild type flt3-L</u>

<u>polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the</u>

<u>mature human wild type flt3-L polypeptide (SEQ ID NO:18) or nucleic acid encoding-such polypeptide</u>.

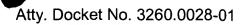
- 44. (Original) The method of claim 43, wherein said disorder is selected from the group consisting of allergy, immunosuppression, and autoimmunity.
- 45. (Currently amended) A method of treating a pathological condition, said method comprising the step of administration of a pharmaceutical composition of a soluble flt3-L mutant polypeptide, wherein said polypeptide comprises a substitution at one or more residues corresponding to amino acid position 24 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) or nucleic acid, and wherein said condition is selected from the group consisting of myelodysplasia, aplastic anemia, Human Immunodeficiency Virus infection, breast cancer, lymphoma, small cell lung cancer, multiple myeloma, neuroblastoma, acute leukemia, testicular cancer and ovarian cancer.

Claims 46-51 (Canceled).

52. (Currently amended) A method of augmenting an immune response in a patient, comprising the step of administering an amount of a <u>soluble</u> flt3-L mutant polypeptide to the patient sufficient to generate an increase in the number of the patient's dendritic cells, wherein said polypeptide comprises a substitution at one or <u>more residues corresponding to amino acid position 24 of the full length human wild 491254 1</u>

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type flt3-L polypeptide (SEQ ID NO:1) or amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

- 53. (Original) The method of claim 52, wherein the patient has an infectious disease.
  - 54. (Original) The method of claim 53, wherein the infectious disease is HIV.
- 55. (Original) The method of claim 52, wherein the patient has a cancerous or neoplastic disease.

Claims 56-68 (Canceled).

- 69. (New) The method according to claim 33, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.
- 70. (New) The method according to claim 69, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).
- 71. (New) The method according to claim <u>33</u>, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.
- 72. (New) The method according to claim 33, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 73. (New) The method according to claim 33, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H 6

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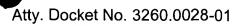


(SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).

- 74. (New) The method according to claim 33, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) and wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 75. (New) The method according to claim 38, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.
- 76. (New) The method according to claim\_75, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).
- 77. (New) The method according to claim 38, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.
- 78. (New) The method according to claim 38, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 79. (New) The method according to claim 38, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H 491254\_1



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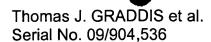


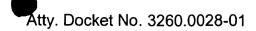
(SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).

- 80. (New) The method according to claim 38, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) and wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 81. (New) The method according to claim 42, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.
- 82. (New) The method according to claim 81, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).
- 83. (New) The method according to claim 42, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.
- 84. (New) The method according to claim 42, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 85. (New) The method according to claim 42, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H 8



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(SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).

- 86. (New) The method according to claim 42, said method comprising administering to said subject a therapeutically effective amount of a pharmaceutical composition comprising a flt3-L mutant polypeptide, wherein said polypeptide comprises a mutation at an amino acid corresponding to position 26, 27, or 64 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 87. (New) The method according to claim 86, wherein said polypeptide comprises a mutation corresponding to L27P (SEQ ID NO:13) or A64T (SEQ ID NO:9).
- 88. (New) The method according to claim 42, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) and wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 89. (New) The method according to claim 43, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.
- 90. (New) The method according to claim 89, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).
- 91. (New) The method according to claim 43, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), 9

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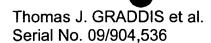
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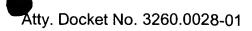
an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.

- 92. (New) The method according to claim 43, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 93. (New) The method according to claim <u>43</u>, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).
- 94. (New) The method according to claim 43, said method comprising administering to said subject a therapeutically effective amount of a pharmaceutical composition comprising a flt3-L mutant polypeptide, wherein said polypeptide comprises a mutation at an amino acid corresponding to position 26, 27 or 64 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 95. (New) The method according to claim 94, wherein said polypeptide comprises a mutation corresponding to L27P (SEQ ID NO:13) or A64T (SEQ ID NO:9).
- 96. (New) The method according to claim 43, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) and wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).



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- 97. (New) The method according to claim 45, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.
- 98. (New) The method according to claim 97, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).
- 99. (New) The method according to claim 45, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.
- 100. (New) The method according to claim 45, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 101. (New) The method according to claim 45, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).
- 102. (New) The method according to claim 45, said method comprising the step of administering of a pharmaceutical composition of flt3-L mutant polypeptide, wherein said polypeptide comprises a mutation at an amino acid corresponding to position 26, 27, or 64 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).
- 103. (New) The method according to claim 102, wherein said polypeptide comprises a mutation selected from L27P (SEQ ID NO:13) or A64T (SEQ ID NO:9).

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104. (New) The method according to claim 45, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1), wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18), and wherein said condition is selected from the group consisting of myelodysplasia, aplastic anemia, Human Immunodeficiency Virus infection, breast cancer, lymphoma, small cell lung cancer, multiple myeloma, neuroblastoma, acute leukemia, testicular cancer, and ovarian cancer.

105. (New) The method according to claim 52, wherein a basic amino acid of the mature human wild type flt3-L polypeptide (SEQ ID NO:18) has been replaced with another amino acid.

106. (New) The method according to claim 105, wherein said basic amino acid is the Lys at position 84 of mature human wild type flt3-L (SEQ ID NO:18).

107. (New) The method according to claim 52, wherein a second polypeptide is fused to the soluble mutant flt3 ligand (flt3-L) polypeptide, wherein said second polypeptide is erythropoietin (EPO), thrombopoietin (TPO), granulocyte-macrophage Colony Stimulating Factor (GM-CSF), granulocyte Colony Stimulating Factor (G-CSF), an interleukin, an immunoglobulin, or fragments thereof, and wherein the fragments retain the biological activity of the second polypeptide.

108. (New) The method according to claim 52, wherein said substitution at one or more residues corresponds to amino acid positions 8, 84, 118, or 122 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

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109. (New) The method according to claim 52, wherein said soluble mutant flt3 ligand (flt3-L) polypeptide comprises one or more substitutions corresponding to L1H (SEQ ID NO:10), H8Y (SEQ ID NO:11), W118R (SEQ ID NO:16), K84E (SEQ ID NO:14), K84T (SEQ ID NO:15), or Q122R (SEQ ID NO:17).

110. (New) The method according to claim 52, wherein said mutant flt3-L polypeptide comprises amino acids 28-160, 28-182, or 28-185 of the full length human wild type flt3-L polypeptide (SEQ ID NO:1) and wherein said mutant flt3-L polypeptide comprises a substitution at one or more residues corresponding to amino acid positions 8-15, 81-87, or 116-124 of the mature human wild type flt3-L polypeptide (SEQ ID NO:18).

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